

analysis very similar to that which he had offered for the large granules that he took to be secretory in liver. Over the next several years, he persisted in referring to the *large granule* fraction, acknowledging that mitochondria were part of the fraction, but continuing to focus on the idea that it also contained secretory granules.

4. LINKING CLAUDE'S MICROSOMES TO PROTEIN SYNTHESIS

Claude's analysis of his "hitherto unrecognized particulate component of protoplasm" – what he called microsomes – indicated the presence of RNA. Although Claude was hesitant to suggest a function for these particles, two other investigators, Jean Brachet and Torbörn Caspersson, led the way. Each deployed new cytochemical tools to establish the connection between RNA and protein synthesis.

Brachet: Selective Staining of RNA and Correlation with Protein Synthesis

While still an undergraduate medical student at the Free University of Brussels in the late 1920s, Brachet tried to determine the location of what was then referred to as thymonucleic acid⁶ (DNA) in growing oocytes. At the time, thymonucleic acid was thought to occur only in animals while zymonucleic acid (RNA) was found primarily in plants (although it was also recognized to be present in the pancreas in animals). The discovery of the Feulgen reaction (Feulgen & Rossenbeck, 1924), which stains DNA green, made it possible for Brachet to try to localize DNA, but it was zymonucleic acid or RNA that was to be the focus of his major breakthrough. Needham and Needham (1930) had found large amounts of nucleic acids in sea urchin eggs, which stained intensely red with pyronine. Was this RNA? Brachet found that when he treated the stained cells with ribonuclease, which specifically digests RNA, this removed the red stain, indicating that it was RNA. Brachet hypothesized, based on the fact that the amount of RNA was closely correlated with protein synthesis activity, that RNA played a role in protein synthesis: "The conclusion to which we are led is that the pentosenucleic acids [RNA] might intervene, by a mechanism as yet obscure, in the synthesis of proteins, which

⁶ The discovery that the substance contained deoxyribose, which led to its rechristening as *deoxyribose nucleic acid* (DNA), only came with the research of Phoebus Levene and Takajiro Mori (1929) at the Rockefeller Institute.